

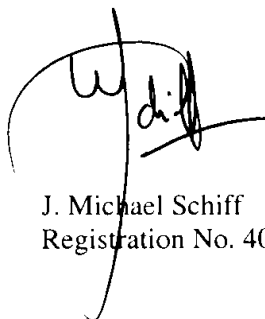
Conclusion

Applicant respectfully requests that all outstanding rejections be reconsidered and withdrawn. The application is believed to be in condition for allowance, and a prompt Notice of Allowance is requested.

In the event that the Examiner determines that there are other matters to be addressed, applicant hereby requests an interview by telephone.

Should the Patent Office determine that an extension of time or any other relief is required for further consideration of this application, applicant hereby petitions for such relief, and authorizes the Assistant Commissioner to charge the cost of such petitions and other fees due in connection with the filing of these papers to Deposit Account No. 07-1139, referencing the docket number indicated above.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "J. Michael Schiff", is written over a large, stylized vertical line that extends from the signature down towards the typed name below.

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## APPENDIX

### ANIMAL TISSUE FOR XENOTRANSPLANTATION

09/593,316  
*Docket 730/002*

#### ***Claims under Examination:***

1. Ovine tissue devoid of antibody-detectable Gal $\alpha$ (1,3)Gal determinants.
2. The tissue of claim 1, which is selected from the group consisting of lung tissue, kidney tissue, liver tissue, cardiac tissue, pancreatic tissue, and ocular tissue.
3. Isolated ovine cell or tissue that expresses glycosyl transferase enzymes but does not detectably express  $\alpha$ (1,3)galactosyltransferase ( $\alpha$ 1,3GT).
4. An ovine cell which is heterozygous or homozygous for inactivation of an  $\alpha$ 1,3GT gene.
5. The cell of claim 4, produced by transfer of a nucleus from a donor cell heterozygous or homozygous for inactivation of an  $\alpha$ 1,3GT gene, to an enucleated recipient cell.
6. An ovine animal that is homozygous for inactivation of an  $\alpha$ 1,3GT gene.
13. A method for producing an ovine that is homozygous for inactivation of an  $\alpha$ 1,3GT gene, comprising providing an ovine embryo of cells according to claim 4, engrafting the embryo into the uterus of a female, birthing an ovine with an inactivated  $\alpha$ 1,3GT gene from the engrafted female, and if the birthed ovine has the  $\alpha$ 1,3GT gene inactivated on only one allele, then mating it with another ovine with an inactivated  $\alpha$ 1,3GT gene, thereby producing an ovine that is homozygous for inactivation of the  $\alpha$ 1,3GT gene.
14. A method for producing an isolated ovine cell that expresses glycosyl transferase enzymes but does not detectably express  $\alpha$ 1,3GT, comprising isolating the cell from an ovine homozygous for inactivation of an  $\alpha$ 1,3GT gene according to claim 6.
15. A method for producing ovine tissue devoid of antibody-detectable Gal $\alpha$ (1,3)Gal determinants, comprising harvesting the tissue from an ovine homozygous for inactivation of an  $\alpha$ 1,3GT gene according to claim 6.
33. The cell of claim 4, which is a fibroblast.
34. The cell of claim 4, which is a kidney cell.
35. The cell of claim 4, which is a hepatocyte.
36. The cell of claim 4, which is a cardiac cell.
37. The cell of claim 4, which is an islet cell.

***Claim for which Rejoinder has been Requested:***

16. A method of xenotransplantation, comprising transplanting tissue devoid of antibody-detectable Gal $\alpha$ (1,3)Gal determinants according to claim 1 into a mammal having circulating antibody against Gal $\alpha$ (1,3)Gal determinants.

***Other Claims Withdrawn from Examination:***

7. A polynucleotide construct effective for inactivating an  $\alpha$ 1,3GT gene in an ovine cell.
17. An isolated polynucleotide that comprises a sequence of at least 30 consecutive nucleotides with at least one of the following properties:
  - a) it is contained in SEQ. ID NO:1 or any of SEQ. ID NOs:14 to 25, but not in any of SEQ. ID NOs: 3, 5, 7, 9, 11, and 13;
  - b) it is contained in phage **B**, **C** and **G** deposited under Accession Nos. NCIMB 41056, 41059, 41060, and 41061; but not in  $\lambda$ -phage or any of SEQ. ID NOs: 3, 5, 7, 9, 11, and 13; or
  - c) it hybridizes under stringent conditions to a polynucleotide with the sequence in SEQ. ID NO:1 or any of SEQ. ID NOs:14 to 25, but not to a polynucleotide with the sequence in any of SEQ. ID NOs: 3, 5, 7, 9, 11, and 13
22. An isolated polypeptide that comprises a sequence of at least 10 consecutive amino acids with at least one of the following properties:
  - a) it is contained in SEQ. ID NO:2 but not in any of SEQ. ID NOs: 4, 6, 8, 10, and 12;
  - b) it is encoded in phage **B**, **C** and **G** deposited under Accession Nos. NCIMB 41056, 41059, 41060, and 41061., but not encoded in  $\lambda$ -phage or present in any of SEQ. ID NOs: 4, 6, 8, 10, and 12; or
  - c) it is at least 80% identical to 15 consecutive amino acids contained in SEQ. ID NO:2, wherein said sequence is not present in any of SEQ. ID NOs: 4, 6, 8, 10, and 12
27. An isolated polynucleotide comprising a sequence encoding a polypeptide according to claim 22.
28. An isolated polyclonal antibody or a monoclonal antibody that binds specifically to a polypeptide with the sequence SEQ. ID NO:2 but not to a peptide with the sequence present in any of SEQ. ID NOs: 4, 6, 8, or 10.
29. An assay method for determining  $\alpha$ 1,3GT expression by a cell, comprising contacting a polynucleotide according to claim 17 with the cell or with mRNA or cDNA obtained from the cell, detecting any hybrids that form as a result, and correlating presence of the hybrids with expression of  $\alpha$ 1,3GT by the cell.
30. A method for producing the antibody specific for sheep  $\alpha$ 1,3GT, comprising immunizing an animal or contacting an immunocompetent particle with a polypeptide according to claim 22.
31. A method for preparing a Gal $\alpha$ (1,3)Gal determinant, comprising contacting a galactose acceptor saccharide with the polypeptide of claim 26 in the presence of UDP-galactose.
32. An assay method for determining  $\alpha$ 1,3GT in a sample, comprising preparing a reaction mixture comprising the sample and an antibody according to claim 28 under conditions that permit the antibody to complex with  $\alpha$ 1,3GT, and correlating any complex formed with the presence or amount of  $\alpha$ 1,3GT in the sample.